REMARKS

Status of the Application

Claims 1-3, 5, 8-12, 16, 18, 19, 23, 25, 27 and 29-48 were pending in the application at the time the Office Action was mailed. Claims 29-48 were rejected. Claims 1-3, 5, 8-12, 16, 18, 19, 23, 25 and 27 were allowed.

By this amendment, claims 29, 30, 34, 35, 39, 42, 44, and 47 have been amended. No claims have been added or canceled. Therefore, claims 1-3, 5, 8-12, 16, 18, 19, 23, 25, 27 and 29-48 remain pending in the application.

Rejections Under 35 U.S.C. 112

Claims 29-48 were rejected under both the written description and enablement sections of 35 U.S.C. 112, first paragraph. Regarding written description, the Office Action states:

> ...the skilled artisan cannot envision the broad genus of devices as claimed because the bacteria comprising appropriate response elements are not disclosed in the specification either explicitly or through a structure-function relationship such that one of skill in the art would know which response elements can necessarily detect a given analyte. The state of the art at the time of filing does not provide sufficient information on the subject to overcome the deficiencies in the instant specification. There is no description in the art that allows one to envision either a singular or plurality of different response elements to detect every known chemical/analyte.

Regarding enablement, the Office Action indicates the specification is enabling for a device enclosed in a water-tight packaging, but argues that the specification does not enable the full scope of the claims essentially because the claimed subject matter is

allegedly in an unpredictable art, that the state of the art provides knowledge of only a few analyte-responsive promoter elements, that the number of working examples and guidance provided by the applicant does not remedy the deficiencies of the state of the art teachings, and that the art is unpredictable and would require a vast amount of empirical experimentation to teach and make the invention as claimed.

The reasoning asserted for both the written description and enablement rejections is that the combined teachings of the specification and state of the art at the time of filing do not describe a sufficient number of analyte-responsive promoters to support the full scope of the claims. Applicants respectfully disagree with this assertion for the reasons set forth below.

Each of the rejected claims includes as an element "cells capable of producing a detectable signal in response to an analyte" (the rejected claims have been amended by replacing "bacteria" with - - cells - -).[1] As indicated by the list of references attached hereto as Appendix A (Abstracts submitted in a supplemental Information Disclosure Statement filed herewith), numerous cells capable of producing a signal in response to an analyte were known prior to the filing date of the present application. For example, a chromosomally-based tod-luxCDABE whole-cell reporter for benzene, toluene, ethybenzene, and xylene sensing (Applegate et al., Appl Environ Microbiol. 64:2730-2735, 1998) was known at the time the application was filed. Because these cells contain the complete lux cassette (luxCDABE), bacterial bioluminescence in response to putative

[1] This element is not limited to cells having an analyte-responsive promoter as the Office Action seems to imply, but rather encompasses any type of cell that might exhibit a signal in response to contact with an analyte (e.g., at a threshold concentration) in a sample.

chemical inducers of the tod operon can be measured in these cells. As another example, bacterial cells containing a cadmium-responsive promoter from E. coli fused to a promoterless lacZ gene were being used to detect environmental pollutants (Biran et al., Environ Microbiol. 2:285-290, 2000) at the time the application was filed. Yet another example includes recombinant yeast cells containing a stable human oestrogen receptor (hER) and a reporter construct comprising an hER response element regulating beta-galactosidase expression (Burdge et al., Analyst. 123:2585-2588, 1998) that were being used to detect oestrogen in bovine plasma at the time the application was filed. Albeit, perhaps, cells do not exist to detect every possible analyte in the universe of different analytes, the claimed subject matter clearly meets the requirements of the written description and enablement portions of 35 USC 112, first paragraph.

With regard to meeting the enablement requirement of 35 U.S.C. 112, first paragraph, MPEP 2164.08 states that "[a]ll that is necessary is that one skilled in the art be able to practice the claimed invention, given the level of knowledge and skill in the art. Further the scope of enablement must only bear a 'reasonable correlation' to the scope of the claims. See, e.g., *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). See MPEP 2164.01 which cites *United States v. Telectronics, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation."). MPEP 2164.01 further states that "[a] patent need not teach, and preferably omits, what is well known in the art." *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann*

Maschinenfabrik GMBH v. American Hoist & Derrick Co., 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984).

Applicant asserts that because of the high level of skill in the art and the state of the art at the time the application was filed, one of ordinary skill in the art would not have to perform undue experimentation to make and use the invention as claimed. Applicant points to the extensive yet not comprehensive list in Appendix A of analyte reporter-detection systems that were known in the art at the time the application was filed.

Regarding the test of enablement, MPEP 2164.05 states that "[t]he state of the prior art provides evidence for the degree of predictability in the art and is related to the amount of direction or guidance needed in the specification as filed to meet the enablement requirement. The state of the prior art is also related to the need for working examples in the specification." Regarding the presence of only one working example (i.e., a mercury response element), MPEP 2164.02 states that "[t]he presence of only one working example should never be the sole reason for rejecting claims as being broader than the enabling disclosure, even though it is a factor to be considered along with all the other factors. To make a valid rejection, one must evaluate all the facts and evidence and state why one would not expect to be able to extrapolate that one example across the entire scope of the claims." Although only one example of an analyte detection-reporter system was described in the application, many such systems were widely known in the art at the time the application was filed. Applicant asserts that the example in the instant application of detecting mercury as an analyte using the claimed device, coupled with the level of skill in the art and the prior art at the time the application was filed, enables one skilled in the art to make and use the claimed invention.

Because there was considerable direction and guidance in the specification as filed, a high level of skill in the art at the time the application was filed, and all of the methods needed to practice the invention were well known, it would not require undue experimentation from one of skill in the art to obtain reporter cells containing a response element corresponding to an analyte of interest needed to practice the claimed invention.

Regarding written description, the analysis of whether the specification complies with the written description requirement is conducted from the standpoint of one of skill in the art at the time the application was filed (see, e.g., *Wang Labs. v. Toshiba corp.*, 993 F.2d 858, 865, 26 USPQ2d 1767, 1774 (Fed. Circ. 1993)) and should include a determination of the field of the invention and the level of skill and knowledge in the art. See, e.g., *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379-80, 231 USPQ 81, 90 (Fed. Cir. 1986). The description need only describe in detail that which is new or not conventional. See *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1384, 231 USPQ at 94; Fonar *Corp. v. General Electric Co.*, 107 F.3d at 1549, 41 USPQ2d at 1805. What is conventional or well known in the art need not be disclosed in detail. See *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d at 1384, 231 USPQ at 94. If a skilled artisan would have understood the inventor to be in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate description requirement is met. See, e.g., *Vas-Cath*, 935 F.2d at 2563, 19 USPQ2d at 1116; *Martin v. Johnson*, 454 F.2d 746, 751, 172 USPQ 391, 395 (CCPA 1972).

Because analyte-detection systems and methods for implementing such systems in many different organisms were widely known in the art at the time the application was

filed (See Appendix A), one of skill in the art would recognize that the inventor was in possession of the invention as claimed in view of the disclosure of the application as filed and therefore a rejection of the claims under 35 U.S.C. 112, first paragraph, is inappropriate. See, e.g., *Vas-Cath, Inc.*, 935 F.2d at 1563-64, 19 USPQ2d at 1117. Because the specification teaches that placing a response element upstream of a reporter gene confers upon the bacterium the ability to respond to an analyte by producing a detectable signal, a skilled artisan would easily envision a response element corresponding to an analyte of interest. This skilled artisan would also readily understand that by placing the response element in the cells of the invention via conventional, well-known molecular cloning methods, the device of the invention could be used to detect a signal in response to the analyte of interest. Therefore, the written description requirement in which a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention, has been met. See, e.g., *Moba, B.V. v. Diamond Automation, Inc.*, 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Circ. 2003); Vas-Cath, Inc. v. Mahurkar, 935 F.2d at 1563, 19 USPQ2d at 1116.

Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation

between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. See *Regents of the University of California v. Eli Lily & Co.*, 119 F.3d at 1568, 43 USPQ2d at 1406.

A "representative number of species" means that the species which are adequately described are representative of the entire genus. There may be situations where one species adequately supports a genus. See, e.g., *Rasmussen*, 650 F.2d at 1214, 211 USPQ at 326-27; *In re Herschler*, 591 F.2d 693, 697, 200 USPQ 711, 714 (CCPA 1979); *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 285 (CCPA 1973). What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. *In re Bell*, 991 F.2d 781, 785, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and *In re Baird*, 16 F.3d 380, 382, 29 USPQ2d 1550, 1552 (Fed. Circ. 1994).

Because the level of skill and knowledge in the art at the time the application was filed was high, and analyte reporter-detection systems were widely known in the art at the time the application was filed (See Appendix A), one of skill in the art would recognize

that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. The detection of mercury as an analyte, as described in the instant application, adequately supports the claimed genus.

For these reasons, the enablement and written description requirements of 35 U.S.C. 112 for each of the pending claims has been satisfied. Accordingly, withdrawal of these rejections and allowance of all pending claims is respectfully requested.

Conclusion

The currently pending claims before the examiner are supported throughout the specification and are patentable over the prior art. No new matter has been added. This application is now in full condition for allowance, and such action is respectfully requested.

The Commissioner is hereby authorized to charge the required fee for a retroactive extension of time and any underpayment or credit any overpayment of fees under 37 CFR 1.16 or 1.17 as required by this paper to Deposit Account 50-3110.

The examiner is cordially invited to call the undersigned if clarification is needed on any matter within this amendment, or if the examiner believes a telephone interview would expedite the prosecution of the subject application to completion.

Respectfully submitted,

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APPENDIX A

1. Applegate et al., A chromosomally based tod-luxCDABE whole-cell reporter for benzene, toluene, ethybenzene and xylene (BTEX) sensing, Appl Environ Microbiol., 1998 July; 64(7): 2730-5.

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